SUMMARY OF PENDING CLAIMS

1. (Three times amended) A method of inhibiting growth of a p53-positive tumor cell in a [mammlian] mammalian subject with a solid tumor comprising the steps of :

(a) providing a viral expression construct comprising a promoter functional in eukaryotic cells and a polynucleotide encoding a functional p53 polypeptide, wherein said polynucleotide is positioned sense to and under the control of said promoter; and

(b) directly administering said viral expression construct to said tumor *in vivo*, the administration resulting in expression of said functional p53 polypeptide in cells of said tumor and inhibition of tumor cell growth,

wherein said tumor comprises cells that express a functional p53 polypeptide.

2. The method of claim 1, wherein said tumor is selected from the group consisting of a carcinoma, a glioma, a sarcoma, and a melanoma.

3. The method of claim 1, wherein said tumor cell is malignant.

4. The method of claim 1, wherein said tumor cell is benign.

5. The method of claim 1, wherein said tumor is a tumor of the lung, skin, prostate, liver, testes, bone, brain, colon, pancreas, head and neck, stomach, ovary, breast or bladder.

6. The method of claim 1, wherein said viral expression construct is selected from the group consisting of a retroviral vector, an adenoviral vector and an adeno-associated viral vector.

7. The method of claim 6, wherein said viral vector is a replication-deficient adenoviral vector.

8. The method of claim 7, wherein said replication-deficient adenoviral vector is lacking at least a portion of the E1-region.

9. The method of claim 8, wherein said promoter is a CMV IE promoter.

10. The method of claim 1, wherein said subject is a human.

11. The method of claim 7, wherein the expression vector is administered to said tumor at least a second time.

12. The method of claim 11, wherein said tumor is resected following at least a second administration, and an additional administration is effected subsequent to said resection.

13. The method of claim 1, wherein said expression vector is administered in a volume of about 3 ml. to about 10 ml.

14. (Amended) The method of claim 11, wherein the amount of adenovirus [administered] in each [contacting] administration is between about 10^7 and 10^{12} pfu.

16. The method of claim 1, wherein the expression construct is injected into a natural or artificial body cavity.

17. The method of claim 16, wherein said injection comprises continuous perfusion of said natural or artificial body cavity.

18. The method of claim 16, wherein said contacting is via injection into an artificial body cavity resulting from tumor excision.

19. The method of claim 1, wherein the *p53*-encoding polynucleotide is tagged so that expression of *p53* from said expression vector can be detected.

20. The method of claim 19, wherein the tag is a continuous epitope.

26. The method of claim 1, wherein said tumor is contacted with said expression construct at least twice.

27. The method of claim 26, wherein said multiple injections comprise about 0.1-0.5 ml volumes spaced about 1 cm apart.

28. The method of claim 1, further comprising contacting said tumor with a DNA damaging agent.

29. The method of claim 28, wherein said DNA damaging agent is a radiotherapeutic agent.

30. The method of claim 29, wherein said radiotherapeutic agent is selected from the group consisting of γ-irradiation, x-irradiation, uv-irradiation and microwaves.

31. The method of claim 28, wherein said DNA damaging agent is a chemotherapeutic agent.

32. The method of claim 31, wherein said chemotherapeutic agent is selected from the group consisting of adriamycin, 5-fluorouracil, etoposide, camptothecin, actinomycin-D, mitomycin C, verapamil, doxorubicin, podophyllotoxin and cisplatin.

33. The method of claim 1, further comprising contacting said tumor with a cytokine.

34. (Canceled) The method of claim 1, further comprising contacting said tumor with a second therapeutic gene other than a gene encoding a *p53* polypeptide.

35. (Canceled) The method of claim 34, wherein said second therapeutic gene is selected from the group consisting of a Dp gene, p21, p16, p27, E_2F, Rb, APC, DC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, FCC, MCC, *ras*, *myc*, *neu*, *raf*, *erb*, *src*, *fms*, *jun*, *trk*, *ret*, *gsp*, *hst*, *bcl*, *abl*, Bax, Bcl-X_s and E1A.

36. The method of claim 1, wherein said tumor is located into a body cavity selected from the group consisting of the mouth, pharynx, esophagus, larynx, trachea, pleural cavity, peritoneal cavity, bladder interior and colon lumen.

37. The method of claim 11, wherein said tumor is contacted with said expression construct at least six times within a two week treatment regimen.

38. A method for inhibiting microscopic residual tumor cell growth in a mammalian subject comprising the steps of:

(a) identifying a mammalian subject having a resectable tumor:

(b) resecting said tumor; and

(c) administering to a tumor bed revealed by resection a viral expression construct comprising a promoter functional in eukaryotic cells and a polynucleotide encoding a functional p53 polypeptide, wherein said polynucleotide is positioned sense to and under the control of said promoter, the administration resulting in expression of said functional p53 polypeptide in said tumor cells and inhibition of their growth.

39. The method of claim 38, wherein said resectable tumor is a squamous cell carcinoma.

40. The method of claim 38, wherein the endogenous *p53* of said resectable tumor is mutated.

41. The method of claim 38, wherein the endogenous *p53* of said resectable tumor is wild-type.

42. The method of claim 38, wherein said tumor is a tumor of the lung, skin, prostate, liver, testes, bone, brain, colon, pancreas, head and neck, stomach, ovary, breast or bladder.

43. The method of claim 38, wherein said viral expression construct is selected from the group consisting of a retroviral vector, an adenoviral vector and an adeno-associated viral vector.

44. The method of claim 43, wherein said adenoviral vector is a replication-deficient adenoviral vector.

45. The method of claim 44, wherein said replication-deficient adenoviral vector is lacking at least a portion of the E1-region.

46. The method of claim 38, wherein said promoter is a CMV IE promoter.

47. The method of claim 38, wherein the resulting tumor bed is contacted with said expression construct at least twice.

48. The method of claim 38, wherein said expression construct is contacted with said tumor bed prior to closing of the incision.

49. The method of claim 44, wherein said the tumor bed is contacted with from about 10^6 to about 10^9 infectious adenoviral particles.

50. The method of claim 47, further comprising contacting said tumor with said expression construct prior to resecting said tumor.

51. The method of claim 50, wherein said tumor is injected with said expression construct.

52. The method of claim 51, wherein said tumor is injected with about 10^6 to about 10^9 infectious adenoviral particles.

53. The method of claim 51, wherein said tumor is injected with a total of about 1 ml to about 10 ml.

54. The method of claim 51, wherein said tumor is injected at least twice.

55. The method of claim 54, wherein each of said injections comprise about 0.1 ml to about 0.5 ml volumes spaced about 1 cm apart.

56. The method of claim 38, wherein the resulting tumor bed is contacted with said expression construct through a catheter.

57. The method of claim 54, wherein said contacting comprises about 10^6 to about 10^9 infectious adenoviral particles.

58. The method of claim 54, wherein said expression construct is contacted with said tumor in total of about 3 ml to about 10 ml.

59. The method of claim 38, wherein the *p53* polynucleotide is tagged so that expression of a *p53* polypeptide can be detected.

60. The method of claim 59, wherein the tag is a continuous epitope.

61. The method of claim 38, further comprising contacting said tumor with a DNA damaging agent.

62. The method of claim 61, wherein said DNA damaging agent is contacted before resection.

63. The method of claim 61, wherein said DNA damaging agent is contacted after resection.

64. (Amended) The method of claim 61, wherein said DNA damaging agent is contacted [contacting] before and after resection.

65. The method of claim 61, wherein said DNA damaging agent is a radiotherapeutic agent.

66. The method of claim 65, wherein said radiotherapeutic agent is selected from the group consisting of γ-irradiation, x-irradiation, uv-irradiation and microwaves.

67. The method of claim 61, wherein said DNA damaging agent is a chemotherapeutic agent.

68. The method of claim 67, wherein said chemotherapeutic agent is selected from the group consisting of adriamycin, 5-fluorouracil, etoposide, camptothecin, actinomycin-D, mitomycin C, verapamil, doxorubicin, podophyllotoxin and cisplatin.

69. The method of claim 38, further comprising contacting said tumor with a cytokine.

70. The method of claim 69, wherein said cytokine is selected from the group consisting of IL-1α, IL-1β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, TGF-β, GM-CSF, M-CSF, TNFα, TNFβ, LAF, TCGF, BCGF, TRF, BAF, BDG, MP, LIF, OSM, TMF, PDGF, IFN-α, IFN-β and IFN-γ.

71. (Canceled) The method of claim 38, further comprising contacting said tumor with a second therapeutic gene other than a gene encoding a *p53* polypeptide.

72. (Canceled) The method of claim 71, wherein said second therapeutic gene is selected from the group consisting of a Dp gene, p21, p16, p27, E_2F, Rb, APC, DC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, FCC, MCC, *ras*, *myc*, *neu*, *raf*, *erb*, *src*, *fms*, *jun*, *trk*, *ret*, *gsp*, *hst*, *bcl*, *abl*, Bax, Bcl-X_s and E1A.

73. The method of claim 38, wherein said tumor is located into a body cavity selected from the group consisting of the mouth, pharynx, esophagus, larynx, trachea, pleural cavity, peritoneal cavity, bladder interior and colon lumen.

74. A method for inhibiting growth of a p53-positive tumor cell in a mammalian subject having a solid tumor comprising the steps of:

(a) surgically revealing said tumor; and

(b) directly administering to said tumor a viral expression construct comprising a promoter functional in eukaryotic cells and a polynucleotide encoding a functional p53 polypeptide, wherein said polynucleotide is positioned sense to and under the control of said promoter, the administration resulting in expression of said functional p53 polypeptide in said tumor cells and inhibition of their growth.

75. The method of claim 74, wherein said tumor is malignant.

76. The method of claim 74, wherein said tumor is a squamous cell carcinoma.

77. The method of claim 74, wherein said tumor is benign.

80. The method of claim 74, wherein said tumor is a tumor of the lung, skin, prostate, liver, testes, bone, brain, colon, pancreas, head and neck, stomach, ovary, breast or bladder.

81. The method of claim 74, wherein said viral expression construct is selected from the group consisting of a retroviral vector, an adenoviral vector and an adeno-associated viral vector.

82. The method of claim 81, wherein said adenoviral vector is a replication-deficient adenoviral vector.

83. The method of claim 82, wherein said replication-deficient adenoviral vector is lacking at least a portion of the E1-region.

84. The method of claim 74, wherein said promoter is a CMV IE promoter.

85. The method of claim 74, wherein said tumor is contacted with said expression construct at least twice.

86. The method of claim 74, wherein said expression construct is contacted with said tumor prior to close of the incision.

87. The method of claim 82, wherein said tumor is contacted with from about 10^6 to about 10^9 infectious adenoviral particles.

88. The method of claim 74, wherein said tumor is contacted with said expression construct in a total of about 1 ml to about 10 ml.

89. The method of claim 74, wherein said tumor is injected at least twice.

90. The method of claim 89, wherein each of said injections comprise about 0.1 ml to about 0.5 ml volumes spaced about 1 cm apart.

91. The method of claim 74, wherein said tumor is contacted with said expression construct through a catheter.

92. The method of claim 91, wherein said tumor is contacted with about 10^6 to about 10^9 infectious adenoviral particles.

93. The method of claim 91, wherein said tumor is contacted with an expression construct in a total of about 3 ml to about 10 ml.

94. The method of claim 74, wherein the *p53* polynucleotide is tagged so that expression of a *p53* polypeptide can be detected.

95. The method of claim 94, wherein the tag is a continuous epitope.

96. The method of claim 74, further comprising contacting said tumor with a DNA damaging agent.

97. The method of claim 96, wherein said DNA damaging agent is contacted with said tumor before resection.

98. The method of claim 96, wherein said DNA damaging agent is contacted with said tumor after resection.

99. The method of claim 96, wherein DNA damaging agent is contacted with said tumor before and after resection.

100. The method of claim 96, wherein said DNA damaging agent is a radiotherapeutic agent.

101. The method of claim 100, wherein said radiotherapeutic agent is selected from the group consisting of γ-irradiation, x-irradiation, uv-irradiation and microwaves.

102. The method of claim 96, wherein said DNA damaging agent is a chemotherapeutic agent.

103. The method of claim 102, wherein said chemotherapeutic agent is selected from the group consisting of adriamycin, 5-fluorouracil, etoposide, camptothecin, actinomycin-D, mitomycin C, verapamil, doxorubicin, podophyllotoxin and cisplatin.

104. The method of claim 74, further comprising contacting said tumor with a cytokine.

105. The method of claim 104, wherein said cytokine is selected from the group consisting of IL-1α, IL-1β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, TGF-β, GM-CSF, M-CSF, TNFα, TNFβ, LAF, TCGF, BCGF, TRF, BAF, BDG, MP, LIF, OSM, TMF, PDGF, IFN-α, IFN-β, and IFN-γ.

106. (Canceled) The method of claim 74, further comprising contacting said tumor with a second therapeutic gene other than a gene encoding a *p53* polypeptide.

107. (Canceled) The method of claim 106, wherein said second therapeutic gene is selected from the group consisting of a Dp gene, p21, p16, p27, E_2F, Rb, APC, DC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, FCC, MCC, *ras*, *myc*, *neu*, *raf*, *erb*, *src*, *fms*, *jun*, *trk*, *ret*, *gsp*, *hst*, *bcl*, *abl*, Bax, Bcl-X_s and E1A.

108. The method of claim 74, wherein said tumor is located in a body cavity selected from the group consisting of the mouth, pharynx, esophagus, larynx, trachea, pleural cavity, peritoneal cavity, bladder interior and colon lumen.

109. (Twice amended) A method of inhibiting tumor cell growth in a mammalian subject having a solid tumor comprising the step of [continuously] catheterizing and perfusing a tumor site in said patient with a viral expression construct comprising a promoter functional in eukaryotic cells and a polynucleotide encoding a functional p53 polypeptide, wherein said polynucleotide is positioned sense to and under the control of said promoter, the administration resulting in expression of said functional p53 polypeptide in cells of said tumor and inhibition of their growth.

110. The method of claim 109, wherein said tumor is malignant.

111. The method of claim 109, wherein said tumor is a squamous cell carcinoma.

112. The method of claim 109, wherein said tumor is benign.

113. The method of claim 109, wherein the endogenous *p53* of said tumor is mutated.

114. The method of claim 109, wherein the endogenous *p53* of said tumor is wild-type.

115. The method of claim 109, wherein said tumor is a tumor of the lung, skin, prostate, liver, testes, bone, brain, colon, pancreas, head and neck, stomach, ovary, breast or bladder.

116. The method of claim 116, wherein said viral expression construct is selected from the group consisting of a retroviral vector, an adenoviral vector and an adeno-associated viral vector.

117. The method of claim 116, wherein said adenoviral vector is a replication-deficient adenoviral vector.

118. The method of claim 117, wherein said replication-deficient adenoviral vector is lacking at least a portion of the E1-region.

119. The method of claim 109, wherein said promoter is a CMV IE promoter.

120. The method of claim 109, wherein said tumor site is perfused from about one to two hours.

121. The method of claim 109, wherein said subject is a human.

122. The method of claim 109, wherein said tumor site is contacted with said expression vector through a catheter.

123. The method of claim 109, wherein the *p53* polynucleotide is tagged so that expression of a *p53* polypeptide can be detected.

124. The method of claim 123, wherein the tag is a continuous epitope.

125. The method of claim 109, further comprising contacting said tumor with a DNA damaging agent.

126. The method of claim 125, wherein said tumor site is contacted with said DNA damaging agent before resection.

127. The method of claim 125, wherein said tumor site is contacted with said DNA damaging agent after resection.

128. The method of claim 125, wherein said tumor site is contacted with said DNA damaging agent before and after resection.

129. The method of claim 125, wherein said DNA damaging agent is a radiotherapeutic agent.

130. The method of claim 129, wherein said radiotherapeutic agent is selected from the group consisting of γ-irradiation, x-irradiation, uv-irradiation and microwaves.

131. The method of claim 125, wherein said DNA damaging agent is a chemotherapeutic agent.

132. The method of claim 131, wherein said chemotherapeutic agent is selected from the group consisting of adriamycin, 5-fluorouracil, etoposide, camptothecin, actinomycin-D, mitomycin C, verapamil, doxorubicin, podophyllotoxin and cisplatin.

133. The method of claim 109, further comprising contacting said tumor with a cytokine.

134. The method of claim 133, wherein said cytokine is selected from the group consisting of IL-1α, IL-1β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, TGF-β, GM-CSF, M-CSF, TNFα, TNFβ, LAF, TCGF, BCGF, TRF, BAF, BDG, MP, LIF, OSM, TMF, PDGF, IFN-α, IFN-β, and IFN-γ.

135. (Canceled) The method of claim 74, further comprising contacting said tumor with a second therapeutic gene other than a gene encoding a *p53* polypeptide.

136. (Canceled) The method of claim 135, wherein said second therapeutic gene is selected from the group consisting of a Dp gene, p21, p16, p27, E_2F, Rb, APC, DC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, FCC, MCC, *ras*, *myc*, *neu*, *raf*, *erb*, *src*, *fms*, *jun*, *trk*, *ret*, *gsp*, *hst*, *bcl*, *abl*, Bax, Bcl-X_s and E1A.

137. The method of claim 109, wherein said tumor is located into a body cavity selected from the group consisting of the mouth, pharynx, esophagus, larynx, trachea, pleural cavity, peritoneal cavity, bladder interior and colon lumen.

138. The method of claim 1, wherein said expression vector is administered topically.

139. The method of claim 1, wherein said expression vector is administered intratumorally.

140. (Canceled) The method of claim 1, wherein said expression vector is administered intravenously.

141. (Canceled) The method of claim 1, wherein said expression vector is administered orally.

142. The method of claim 74, wherein said expression vector is administered topically.

143. The method of claim 74, wherein said expression vector is administered intratumorally.

144. (Canceled) The method of claim 74, wherein said expression vector is administered intravenously.

145. (Canceled) The method of claim 74, wherein said expression vector is administered orally.